Data pooling opportunities
In visceral leishmaniasis

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ECTMIH - Basel
Value of individual patient data sharing

• Maintains research data in useful formats
  – Understand and apply new knowledge gained, even decades after studies are originally conducted

• When standardised, power of pooled data
  – Increase statistical power
  – Test new hypotheses, improve methodologies

• An essential tool for disease elimination
  – What is the scale of the problem?
  – What is the optimal way to control – eliminate – eradicate?
Pooling individual patient data

Innovate
Address heterogeneity
Collate/Collect
WWARN Mission: Reliable evidence for decisions

- Multidisciplinary & scientifically independent
  - Providing high-quality analysis
  - Practical research tools and services
  - A forum for partnership
    - over 250 collaborators across the world
- Enhance collaboration among researchers
  - To pool and analyse data on drug **efficacy** to answer questions of public health importance

[www.wwarn.org](http://www.wwarn.org) 2/3 of the ACT efficacy trial data from around the world
Impact ➔ Evidence

Dose Impact Study Group results:

- Dihydroartemisinin-Piperaquine: new dosage recommendations
- Artesunate-Amodiaquine: Evidence on higher efficacy of fixed combination
- Artemether-Lumefantrine: concerns for the treatment of malnourished children
- Correlation between molecular markers and clinical efficacy
Standardization and scalability

**Ethical & Legal framework**

Data Repository

- **Cleanse**
- **Transform**
- **Standardize**
- **Analyse**

Data sharing

Processing

Outputs

Heterogeneous data

Access

Stata

SAS

Excel

Standardized report to contributor

Standardized data sets

WWARN Explorer

Research applications
Visceral leishmaniasis data sharing platform rationale

- Sufficient data to consider such platform?
  - Technical feasibility
    - Data structure
    - Data standardisation
    - Methodological issues
  - What would it take?
    - Stakeholders interests

Systematic data review
Methodology

• Search `Visceral leishmaniasis` and `Kala azar`
• Exclude
  – Trials on vaccines, canine VL, vector control, nets, prevalence estimation,
  – Diagnostic tests
  – Prophylaxis
  – Cutaneous leishmaniasis
Systematic data review

Trial repositories

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

World Health Organization

33 registered trials

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13 of 33 registered trials are published

- Active: 11 trials
- Terminated: 3 trials
- Complete not published: 6 trials
Published literature
Search `Visceral leishmaniasis` and `Kala azar`

13 of 33 registered trials are published

141 published trials
- 126 Published
- 15 Published and registered

Systematic data review

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

World Health Organization
International Clinical Trials Registry Platform

NCBI Resources
PubMed.gov

THE COCHRANE LIBRARY
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Clinical trials landscape

- 141 clinical studies on VL drugs,
  - 25,865 patients (68% male)
  - Most trials enroll less than 200
- 1,379 patients in completed, unpublished trials and 9,802 in active trials
  - Total > 37,000 patients
Where and when?

Number of trials by region:
- Indian subcontinent: 98
- Africa: 22
- Mediterranean: 12
- Brazil: 5
- Central Asia: 3
- Across regions: 1

Cumulative enrolment by region:
- Indian subcontinent: 21216
- Africa: 3991

Technical feasibility

Across regions,
Drugs

- 2000-6000 patients enrolled for each drug
  - Large scale comparisons potentially possible
  - Limited variation of dosages

- Most enrollments for newer drugs are recent (5-10 years)
  → Easier to obtain data
Trial designs

- Trials evenly split between single arm, dose finding or comparative

- Most patients followed up for
  - 6 months (~25,000)
  - Some for 12 months (~5000)

- Allows pooling of data since end points consistent
  - Comparison between 12 and 6 months follow up

Technical feasibility

- Single arm; 50; 35%
- Dose finding Randomized, 32, 23%
- Comparative, 28%
- Dose finding, 37%
Restrospective data: main findings

- Individual trials are in general small scale but
  - In total many trials (141)
  - Potential for 37,000 patients
- Good consistency in trial design and parameters
- Meta-analysis would allow comparisons on large patient cohorts (1000`s per arm) to improve treatment selection and inform design of future trials
- Enhance drug development
  - Speeding up the availability of outcomes
Pilot phase

- Michael Otieno (one year fellowship)
- Technical feasibility
  - No major obstacles
- Develop a pilot platform
  - Web-interface
  - Adapt standardisation tools
  - Legal & ethical framework to operate
  - Prospective data collection
- Respond to stakeholders’ needs
Why pooling data critical for NTDs?

• Tropical medicine versus others
  – Lower data volume
  – Challenges to recruit patients
  – Limited commercial interest

• Perception of data ownership is challenged by recent data sharing policies developed by funding agencies
  – Disadvantage for developing countries’ PIs
  – Incentive to engage primary data contributors in data sharing essential for success
  – Responsible data sharing platform
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